

the recitation of "about" from before the "3%" limitation in claims 1, 18 and 27. It is urged that the recitation of "about 0.1%" is definite and justified and would not cause any confusion to the ordinary artisan.

It is submitted that the recitation of "about 0.1%" is justified and proper. Chain-shortened 2'-5' polynucleotides in which a phosphate rearrangement rate is less than 0.1% should not be judged to be outside the patent if the "about" was deleted, and applicants urge that they are entitled to a patent with less than 0.1% except for 0%. In addition, Applicants submit that the error in measuring of the phosphate rearrangement rate should be taken into consideration.

Applicants believe that the recitation of "about 0.1%" is definite.

Applicants found that the activity of the chain-shortened polynucleotide correlates closely with the phosphate rearrangement rate. The lower the phosphate rearrangement rate, the higher the activity (e.g., see Test Example 3 in the present application). In the present specification, the chain-shortened polynucleotide in which the phosphate rearrangement rate is less than 0.1% is not disclaimed. The present specification mentions 3% or less, or 2% or less firstly before mentioning between 0.1% and 3%, or between 0.1% is not disclaimed. The present specification mentions 3% or less, or 2% or less firstly before mentioning between 0.1% and 3%, or between 0.1% and 2% (e.g., see lines polynucleotide in which the phosphate rearrangement rate is 0% does not have novelty. Those skilled in the art understand that when a polynucleotide is chain-shortened with an enzyme, not by hydrolysis, a chain-shortened polynucleotide in which the phosphate rearrangement rate is 0% can be produced.

Applicants describe the lower limit of the phosphate rearrangement rate tentatively as 0.1% in the present specification. The "0.1%" simply means that the phosphate rearrangement rate does not contain 0%.

For the above reasons, applicants urge reconsideration and withdrawal of this § 112, second paragraph formal objection.

**Claim Rejection 35 USC § 102**

Claims 1, 7, 10, 14, 16, 18, 19, 23 and 24 have been rejected under 35 USC § 102 (b) as allegedly being anticipated by Xiao et al (Xiao).

Claims 1, 7 and 17 have been rejected under 35 USC § 102 (e) as allegedly being anticipated Kandimalla et al (Kandimalla).

Applicants respectfully traverse both of these rejections.

In both of these rejections, the Examiner states that the recitation of "about 3%" in the present claims may cause the present claims to be anticipated by the cited references even though the references do not teach or disclose any nucleotides which have 2'-5'- phosphodiester linkages within the range of about 0.1% to 3%. A reference in order to be a proper anticipation must exactly disclose all of the elements of the claims against which the reference is applied. Such is not the case herein in as much as neither cited reference either teaches or discloses materials such as recited in the instant claims. This is especially the case since the present claims no longer use the term "about 3%".

Applicants request reconsideration and withdrawal of the § 102 rejections.

**Claim Rejections – 35 USC § 103**

Claims 2, 3, 6, 8, 9, 15, 17, 20, 25 and 26 have been rejected under 35 USC § 103 (a) as allegedly being unpatentable over Xiao in view of Yano et al (Yano) and further in view of Kandimalla.

Claim 14 has been rejected under 35 USC § 103 (a) as allegedly being unpatentable over Xiao, in view of Yano further in view of Kandimalla and Junichi et al (Junichi).

Applicants respectfully disagree with respect to both of these rejections and urge reconsideration by the Examiner.

First of all, the cited "J. Med. Chem." (Guiying) relates to an antisense DNA with 2'-5'- Oligoadenosine inserted on purpose. Kandimalla relates to an antisense DNA with 2' 5' RNA inserted on purpose as well. On the other hand, Yano relates to a double stranded poly I:poly C (a RNA) having activities such as Interferon inducing action, but does not relate to an antisense nucleotide at all. The art taught by Yano is entirely different from the art taught by Guiying mistakenly called Xiao by the Examiner or Kandimalla. Therefore, it is impossible for persons skilled in the art to combine Yano with Guiying or Kandimalla.

If teaching of Yano could have been combined with that of Guiying or Kandimalla, persons skilled in the art could not reach the present invention according to the chain-shortened polynucleotide in which the phosphate rearrangement rate is less than 3%. The phosphate rearrangement rates according to Guiying and Kandimalla are both more than 3%.

In addition, the present invention illustrates that existence of 2' 5' nucleotide is disadvantageous to activity. On the other hand, 2' 5' nucleotides according to Guiying and Kandimalla act advantageously in activity. The 2' 5' nucleotides according to Guiying and Kandimalla are different from that of the present invention in technical meaning. Also Guiying and Kandimalla relate to antisense nucleotide different from the present invention. Therefore, Guiying and Kandimalla cannot fall in relevant prior arts with the present invention. Further, Guiying does not teach a composition comprising a complex formed from a carrier like cationic liposomes and a nucleotide at all.

With regard to US 5795587 (Gao) and US 6020317 (Junichi), both of these patents disclose a cationic liposome useful for the transfer of nucleic acid. Since persons skilled in the art cannot make the present invention by combining Guiying, Yano and Kandimalla, it goes without saying that they cannot also make the invention by combining Gao and/or Junichi with the aforesaid teachings.

For the above reasons, applicants urge that the Examiner's § 103 rejections are in error and reconsideration and withdrawal of both of these rejections is requested.

### **CONCLUSION**

It is urged that all of the present claims are in condition for allowance. Early and favorable action by the Examiner is earnestly solicited.

### **AUTHORIZATION**

If the Examiner believes that issues may be resolved by telephone interview, the Examiner is respectfully urged to telephone the undersigned at (212) 801-2146. The undersigned may also be contacted by e-mail at [ecr@gtlaw.com](mailto:ecr@gtlaw.com).

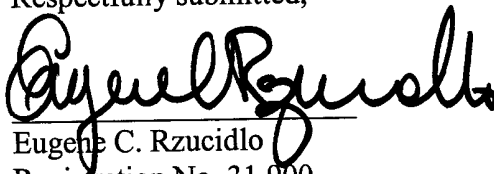
No additional fee is believed to be necessary. The Commissioner is hereby authorized to charge any additional fees which may be required for this amendment, or credit any overpayment to Deposit Account No. 50-1561.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 50-1561.

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Respectfully submitted,

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## ATTACHMENT

1. (Amended) A chain-shortened polynucleotide or salt thereof, comprising phosphodiester bonds, wherein from about 0.1 percent to [about] 3 percent of the phosphodiester bonds are 2'-5' phosphodiester bonds.

18. (Amended) A composition comprising a complex formed from a carrier effective for introducing a medicament into a cell and a chain-shortened polynucleotide or salt thereof as an essential ingredient, wherein the chain-shortened polynucleotide or salt thereof comprises phosphodiester bonds, such that from about 0.1 percent to [about] 3 percent of the phosphodiester bonds are 2'-5' phosphodiester bonds.

27. (Amended) A method for preparing a polynucleotide or salt thereof in which the proportion of a 2'-5' phosphodiester bond is up to [about] 3% based on the total phosphodiester bonds and the average chain length is between 0.1 k bases and 1 k bases comprising measuring the phosphate rearrangement rate in the course of preparing the polynucleotide or salt thereof.